Amendments to the Claims:

Claims 63-73 and 99-106 were cancelled via the Preliminary Amendment of September 26, 2002. On January 30, 2004, Applicants provisionally elected with traverse the invention of Group I, namely claims 1-62. Although the outstanding Office Action indicates that the Office has withdrawn claims 63-106, Applicants believe that, in view of the previous cancellation of claims 63-73 and 99-106, the Office meant to indicate that claims 74-98 have been withdrawn.

Prior to further substantive examination, please cancel pending claims 1-32, 34, 35, and 55 without prejudice to their subsequent reintroduction into this application or their introduction into a related application. Claim 107 has been added. Claims 33, 36, 37, 40-44, 47, 49, 51, 53, 58 and 59 have been amended. Upon entry of this paper, claims 33, 36-54, 56-62, and 107 will be pending and under consideration in this case.

The following listing of claims replaces all prior versions and lists of claims in the application:

Listing of Claims:

1-32. (Cancelled)

33. (Currently Amended) A method of identifying a ~~candidate~~ molecule that binds to a large ribosomal subunit, the method comprising the steps of:

(a) ~~providing a molecular model of a ribofunctional locus of a large subunit of a ribosome, wherein the molecular model is based on atoms derived from an electron density map having a resolution of at least about 4.5 Å; and~~ providing a molecular model comprising one or more target regions selected from the group consisting of at least a portion of (i) a peptidyl transferase site, (ii) an A-site, (iii) a P-site, (iv) an E-site, (v) an elongation factor binding domain, (vi) a polypeptide exit tunnel, and (vii) a signal recognition particle (SRP) binding domain, from the atomic co-ordinates for *Haloarcula marismortui* large ribosomal subunit found on

Disk 1 under file name 1JJ2.RTF, 1JJ2.TXT, 1JJ2.PDB, PDB1FFK.DOC, or PDB1FFK.ENT, or deposited at the Protein Data Bank under accession number PDB ID: 1JJ2 or 1FFK, or derived from said *Haloarcula marismortui* atomic co-ordinates by molecular modeling;

(b) using the molecular model to identify a candidate molecule ~~having a surface complementary to the ribofunctional locus.~~ that can bind to the one or more target regions in the molecular model; and

(c) producing the candidate molecule identified in step (b).

34-35. (Cancelled)

36. (Currently Amended) The method of claim 33 ~~or 35~~, comprising the additional step of determining whether the candidate molecule modulates ribosomal activity.

37. (Currently Amended) The method of claim 36, comprising the additional step of ~~identifying~~ repeating one or more of steps (a) through (c) to identify a modified molecule.

38. (Original) The method of claim 37, comprising the additional step of producing the modified molecule.

39. (Original) The method of claim 38, comprising the additional step of determining whether the modified molecule modulates ribosomal activity.

40. (Currently Amended) The method of claim 39, comprising the additional step of, after determining whether the modified molecule modulates ribosomal activity, producing the modified molecule.

41. (Currently Amended) The method of claim 33, wherein the candidate molecule is an antibiotic ~~or an antibiotic analogue~~.

42. (Currently Amended) The method of claim 37, wherein the modified molecule is an antibiotic ~~or an antibiotic analogue~~.

43. (Currently Amended) The method of claim 41, wherein the antibiotic ~~or antibiotic analogue~~ is a macrolide.

44. (Currently Amended) The method of claim 33, wherein ~~the ribofunctional locus~~ the one or more target regions comprises at least a portion of an active site.

45. (Original) The method of claim 44, wherein the active site comprises at least a portion of a peptidyl transferase site.

46. (Original) The method of claim 44, wherein the peptidyl transferase site is defined by a plurality of residues set forth in Table 5A or Table 5B.

47. (Currently Amended) The method of claim 33, wherein ~~the ribofunctional locus~~ the one or more target regions comprises at least a portion of an A-site.

48. (Original) The method of claim 47, wherein the A-site is defined by a plurality of residues set forth in Table 6A or Table 6B.

49. (Currently Amended) The method of claim 33 or 47, wherein ~~the ribofunctional locus~~ the one or more target regions comprises a least a portion of a P-site.

50. (Original) The method of claim 49, wherein the P-site is defined by a plurality of residues set forth in Table 7A or Table 7B.

51. (Currently Amended) The method of claim 33 or 47, wherein ~~the ribofunctional locus~~ the one or more target regions comprises at least a portion of a polypeptide exit tunnel.

52. (Original) The method of claim 51, wherein the exit tunnel is defined by a plurality of residues set forth in Table 8A, Table 8B, Table 9, or Table 10.

53. (Currently Amended) The method of claim 49, wherein ~~the ribofunctional locus~~ the one or more target regions comprises at least a portion of a polypeptide exit tunnel.

54. (Original) The method of claim 53, wherein the exit tunnel is defined by a plurality of residues set forth in Table 8A, Table 8B, Table 9, or Table 10.

55. (Cancelled)

56. (Original) The method of claim 33, wherein the molecular model is in an electronic form.

57. (Original) The method of claim 33, wherein the molecular model is generated from atomic co-ordinates produced by molecular modeling.

58. (Currently Amended) The method of claim 33 or 57, wherein the molecular model is generated from atomic co-ordinates produced by homology modeling using at least a portion of the atomic co-ordinates deposited at the Protein Data Bank under accession number PDB ID: 1FFK, 1FFZ, 1FG0, 1JJ2, ~~1K73, 1KC8, 1K8A, 1KD1, or 1K9M~~ or recorded on Disk No. 1 under file name PDB1FFK.DOC, PDB1FFK.ENT, PDB1FFZ.DOC, PDB1FFZ.ENT, PDB1FG0.DOC, PDB1FG0.ENT, 1JJ2.RTF, 1JJ2.TXT, or 1JJ2.PDB.

59. (Currently Amended) The method of claim 33 or 57, wherein the molecular model is generated from atomic co-ordinates produced by molecular replacement using at least a portion of the atomic co-ordinates deposited at the Protein Data Bank under accession number PDB ID: 1FFK, 1FFZ, 1FG0, 1JJ2, ~~1K73, 1KC8, 1K8A, 1KD1, or 1K9M~~ or recorded on Disk No. 1 under file name PDB1FFK.DOC, PDB1FFK.ENT, PDB1FFZ.DOC, PDB1FFZ.ENT, PDB1FG0.DOC, PDB1FG0.ENT, 1JJ2.RTF, 1JJ2.TXT, or 1JJ2.PDB.

60. (Original) The method of claim 33, wherein the molecular model comprises residues that are conserved among one or more prokaryotic organisms.

61. (Original) The method of claim 33, wherein the molecular model comprises a residue that is present in a prokaryotic ribosome but is absent from a eukaryotic ribosome or a eukaryotic mitochondrial ribosome.

62. (Original) The method of claim 61, wherein the eukaryotic ribosome is a mammalian ribosome.

63-73. (Cancelled)

74-98. (Withdrawn)

99-106. (Cancelled)

107. (New) A method of identifying a molecule that binds to a large ribosomal subunit, the method comprising the steps of:

(a) providing a molecular model comprising one or more target regions selected from the group consisting of a peptidyl transferase site, an A-site, a P-site, an E-site, an elongation factor binding domain, a polypeptide exit tunnel, and a signal recognition particle (SRP) binding domain, from the atomic co-ordinates (i) for *Haloarcula marismortui* large ribosomal subunit found on Disk 1 under file name 1JJ2.RTF, 1JJ2.TXT, 1JJ2.PDB, PDB1FFK.DOC, or PDB1FFK.DOC, or deposited at the Protein Data Bank under accession number PDB ID: 1JJ2 or 1FFK, or (ii) derived from the *Haloarcula marismortui* atomic co-ordinates by molecular modeling;

(b) using the molecular model to identify a candidate molecule that can bind to the one or more target regions in the molecular model; and

(c) producing the candidate molecule identified in step (b).